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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,215	08/21/2003	Guenther Adolf	1/1383	8054

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EXAMINER
HUFF, SHEELA JITENDRA

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,215	ADOLF ET AL.	
	Examiner	Art Unit	
	Sheela J Huff	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29,49 and 50* is/are rejected.

7)☒ Claim(s) *30-48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-50 are pending.

Information Disclosure Statement

The IDS filed 12/1/03 has been considered and an initialed copy of the PTO-1449 is enclosed.

Claim Objections

Claims 30-48 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim and/or should refer to the other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims 30-48 have not been further treated on the merits.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 10, "claim9" should be --claim 9--.

Claims 6 and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

The specification lacks complete deposit information for the deposit of hybridoma cell line DSM ACC2174. It is not clear that hybridomas possessing the identical properties of DSM ACC2174 are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed hybridoma cell lines and monoclonal antibodies, this method will not necessarily reproduce antibodies and hybridomas which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive a monoclonal antibody and hybridoma identical to those claimed. Undue experimentation would be required to screen all of the possible antibody and hybridoma species to obtain the claimed antibodies and hybridomas.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed hybridoma, a suitable deposit for patent purposes, evidence of public availability of the claimed hybridoma or evidence of the reproducibility without undue experimentation of the claimed hybridoma, is required.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claims 27 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the cancers listed in claim 36, does not reasonably provide enablement for all cancers. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant claims the treatment of all types of cancers. The antibody used as the targeting agent is only specific for CD44. Not all cancer cells express CD44. Since not all cells express CD44 and since the targeting agent of the instant invention is directed to CD44, it is unlikely that the targeting agent will bind to and treat cancers that do not express CD44. Thus, it is the Examiner's position that undue experimentation would be required by one skilled in the art use the instant invention to treat all types of cancers.

Statutory Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-12 and 21-25 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-18 of copending Application No.10150475 (US 2003/0103985). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-12 and 21-25 are directed to the same invention as that of claims 1-12 and 1-18 of commonly assigned 10150475 (US 2003/0103985). . The issue of priority under 35 U.S.C. 102(g) and possibly 35 U.S.C. 102(f) of this single invention must be resolved.

Since the U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302), the assignee is required to state which entity is the prior inventor of the conflicting subject matter. A terminal disclaimer has no effect in this situation since the basis for refusing more than one patent is priority of invention under 35 U.S.C. 102(f) or (g) and not an extension of monopoly.

Failure to comply with this requirement will result in a holding of abandonment of this application.

Claims 1-12 and 21-25 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 10/150475 which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if published under 35 U.S.C. 122(b) or patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future publication or patenting of the copending application.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not

the invention "by another," or by an appropriate showing under 37 CFR 1.131. This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

Obviousness-type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 26-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-26 and 31-36 of copending Application No. 10150475 (US 2003/0103985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the product in the application has a different scope. In the '215 application, claim 19 requires the maytansinoid to be of the Formula IV, whereas in the instant application the maytansinoid compound can include other derivatives. Furthermore, the antibody in

the'215 application can be any CD44v6 antibody (humanized, chimeric, etc) whereas the antibody in the instant application must be humanized.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 26-29 are directed to an invention not patentably distinct from claims 19-26 and 31-36 of commonly assigned 10/150475. Specifically, the claims in the conflicting cases are not distinct because of the reasons cited above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 10/150475, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Claims 26-29 are rejected under 35 U.S.C. 103(a) as being obvious over US 20030103985 (10/150475).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2). The applications are obvious over each as discussed above..

Claims 1 and 4-6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6, 8-12 of U.S. Patent No. 5916561. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only difference between the two sets of claims is the scope of the compound linked to the antibody. In the instant invention the compound merely needs to be toxic to cells. In the patent the compound can be a polypeptide or radioactive isotope or any other molecule (either toxic or not). Thus the scope of the compound in the patent is broader than that of the instant invention and the compounds of the instant invention fall within the broad scope of the patent's.

Claims 1 and 4-6 directed to an invention not patentably distinct from claims 6 and 8-12 of commonly assigned US 5916561. Specifically, the claimed invention are not distinct for the reasons set forth above..

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned US 5916561, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5916561.

This reference discloses monoclonal antibody VFF-18 and the humanization of VFF-18 and linking the antibody to toxins, prodrugs and radioactive substances for the use of therapy(see col. 2, lines 20-55). It is noted that the sequence of claim 5 is not specifically found in the reference but in view of the fact that it the exact same antibody VFF-18 in the patent and in the instant application, it is inherent that they are specific for the same epitope (ie SEQ ID NO. 3).

Claims 1, 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Heider et al Cancer Immunol. Immunother. (1996) 43:245.

This reference discloses monoclonal antibody VFF-18 and its reaction with squamous cell carcinomas (head and neck, lung and skin) (see abstract) and clearly disclose that tumor-targeting "experiments in a nude mouse model comfirmed the potential of VFF18 for diagnostic and therapeutic use in cancer patients" (p. 246, first column). The antibody is linked to 125I, which is toxic. The conjugate is used in in vivo assays and thus is used in a pharmaceutical composition. It is noted that the sequence of claim 5 is not specifically found in the reference but in view of the fact that it the exact same antibody VFF-18 in the patent and in the instant application, it is inherent that they are specific for the same epitope (ie SEQ ID NO. 3).

Claim Rejections - 35 USC § 101

Claims 28 and 29 provides for the use of maytansiniod, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 28 and 29 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App.

1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5916561.

This reference discloses monoclonal antibody VFF-18 and the humanization of VFF-18 and linking the antibody to toxins, prodrugs and radioactive substances for the use of therapy(see col. 2, lines 20-55). These compounds are used in diagnostic assays and are thus part of a composition (see Examples 3+). It is noted that the sequence of claim 5 is not specifically found in the reference but in view of the fact that it the exact same antibody VFF-18 in the patent and in the instant application, it is expected that they are specific for the same epitope (ie SEQ ID NO. 3).

The only difference between the instant invention and the reference is that the reference does not specifically disclose the sequences in claim 7 nor does the reference disclose the method of treating cancer.

Since the reference clearly suggests humanizing VFF-18 and the instant invention humanizes VFF-18 (ie both the instant application and the reference are humanizing the exact same antibody), one of ordinary skill in the art would immediately envisage the humanized version to be that of the instant application. Furthermore, the reference discloses the use of the diagnostic antibody to diagnose cancers, thus, when the reference discloses therapeutics, one of ordinary skill in the art would immediately envisage the treatments to be directed to cancers.

Thus, in view of the clear suggestions in the reference to humanize VFF-18 and its use in the cancer field, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use VFF-18 linked to toxins to treat cancers.

Claims 1, 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heider et al Cancer Immunol. Immunother. (1996) 43:245.

This reference discloses monoclonal antibody VFF-18 and its reaction with squamous cell carcinomas (head and neck, lung and skin) (see abstract) and clearly disclose that tumor-targeting "experiments in a nude mouse model comfirmed the potential of VFF18 for diagnostic and therapeutic use in cancer patients" (p. 246, first column). The antibody is linked to 125I, which is toxic. The conjugate is used in in vivo assays and thus is used in a pharmaceutical composition. It is noted that the sequence of claim 5 is not specifically found in the reference but in view of the fact that it the exact same antibody VFF-18 in the patent and in the instant application, it is expected that they are specific for the same epitope (ie SEQ ID NO. 3).

The only difference between the instant invention and the reference is that the reference does not specifically show the use of conjugate in the treatment of tumors. However, the reference clear suggests the therapeutic use of the compound as noted above and statement such as "these data suggest that mAb VFF18 is a promising targeting vehicle for radioimmunotherapy of squamous cell carcinomas in humans (bottom of abstract).

Thus, in view of these suggestions, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the conjugate in treatments.

Claims 1-29 and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/24763 in view of Heider et al Cancer Immunol. Immunother. (1996) 43:245 or US 5916561 and applicant's admission on pages 22+ of the specification.

The primary reference discloses immunoconjugates comprising "at least one therapeutic agent for killing selected cell populations linked to a cell binding agent " (p. 4, lines 27) in combination with a known chemotherapeutic agent. The therapeutic agent is a variety of different anti-mitotic agents including maytansinoid (see pages 4-5). Pages 5-15 disclose a multitude of maytansinoid derivatives which read on the maytansinoid in applicant's claims. The bottom of page 5 -6 discloses a variety of different linking groups including the use of disulfide groups. Pages 22-25 of the reference further disclose the known chemotherapeutic agents and these include taxanes such as paclitaxel, docetaxel, and the like, platinum compounds, epidophyllotoxin, camptothecin, epothilone compounds such as A, B, C, D, E, and F and derivatives thereof, cisplatin compounds and the like and microtubule stabilizing agents. (Applicant admits on page 22+ of the spec. that the other chemotherapetuic agnets used in the claims are known in the art).

The only difference between the instant invention and the reference is the targeting agent which is antibody CD44 in that instant application.

On page 17 of the primary reference the reference discloses that the "selection of the appropriate cell binding agent is a matter of choice that depends upon the particular cell population that is to be targeted, but in general monoclonal antibodies are preferred".

US 5916591 discloses monoclonal antibody VFF-18 and the humanization of VFF-18 and linking the antibody to toxins, prodrugs and radioactive substances for the use of therapy(see col. 2, lines 20-55). These compounds are used in diagnostic assays and are thus part of a composition (see Examples 3+). It is noted that the sequence of claim 5 is not specifically found in the reference but in view of the fact that it the exact same antibody VFF-18 in the patent and in the instant application, it is expected that they are specific for the same epitope (ie SEQ ID NO. 3). Since the reference clearly suggests humanizing VFF-18 and the instant invention humanizes VFF-18 (ie both the instant application and the reference are humanizing the exact same antibody), one of ordinary skill in the art would immediately envisage the humanized version to be that of the instant application. Furthermore, the reference discloses the use of the diagnostic antibody to diagnose cancers, thus, when the reference discloses therapeutics, one of ordinary skill in the art would immediately envisage the treatments to be directed to cancers.

Heider et al disclose monoclonal antibody VFF-18 and its reaction with squamous cell carcinomas (head and neck, lung and skin) (see abstract) and clearly disclose that tumor-targeting "experiments in a nude mouse model confirmed the potential of VFF18 for diagnostic and therapeutic use in cancer patients" (p. 246, first

column). The antibody is linked to 125I, which is toxic. The conjugate is used in in vivo assays and thus is used in a pharmaceutical composition. It is noted that the sequence of claim 5 is not specifically found in the reference but in view of the fact that it the exact same antibody VFF-18 in the patent and in the instant application, it is expected that they are specific for the same epitope (ie SEQ ID NO. 3). The reference clearly suggests the therapeutic use of the compound as noted above and in statements such as "these data suggest that mAb VFF18 is a promising targeting vehicle for radioimmunotherapy of squamous cell carcinomas in humans (bottom of abstract).

Thus, both secondary reference are clearly disclosing the use of VFF18 in therapeutic compositions to treat carcinomas. In view of this, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use VFF18 or humanized versions thereof in the immunoconjugates/chemotherapeutic composition of the primary reference with the expected benefits of achieving an immunoconjugate highly specific for cells expressing CD44.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Tuesday 5:30am-11:30am and Fridays 6:00am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheela J Huff
Primary Examiner
Art Unit 1642

sjh